

**AMENDMENTS****In the Specification:**

*Page 4, please replace the paragraph starting on line 13, with the following amended paragraph:*

Fig. 1 shows the result of liquid chromatography in the liquid chromatography (LC)-mass spectrometry (MS) of the peptide fragment SLSLSP (SEQ ID NO: 3), in which the top graph is a chromatogram detected by a UV at 215 nm and the bottom graph is a base peak chromatogram.

*Page 4, please replace the paragraph starting on line 18, with the following amended paragraph:*

Fig. 2 shows a mass spectrum in the liquid chromatography (LC)-mass spectrometry (MS) of the peptide fragment SLSLSP (SEQ ID NO: 3).

*Page 4, please replace the paragraph starting on line 21, with the following amended paragraph:*

Fig. 3 shows a zoom scan spectrum in the liquid chromatography (LC)-mass spectrometry (MS) of the peptide fragment SLSLSP (SEQ ID NO: 3).

*Page 4, please replace the paragraph starting on line 24, with the following amended paragraph:*

Fig. 4 shows the result of liquid chromatography in the liquid chromatography (LC)-mass spectrometry (MS) of the peptide fragment SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4), in which the top graph is a chromatogram detected by a UV at 215 nm and the bottom graph is a base peak chromatogram.

*Page 4, please replace the paragraph starting on line 29, with the following amended paragraph:*

Fig. 5 shows a mass spectrum in the liquid chromatography (LC)-mass spectrometry (MS) of the peptide fragment SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4).

*Page 4, please replace the paragraph starting on line 32, with the following amended paragraph:*

Fig. 6 shows a zoom scan spectrum in the liquid chromatography (LC)-mass spectrometry (MS) of the peptide fragment SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4).

*Page 4, please replace the paragraph starting on line 35, with the following amended paragraph:*

Fig. 7 shows the result of liquid chromatography in the liquid chromatography (LC)-mass spectrometry (MS) of the mixture of the peptide fragments SLSLSP (SEQ ID NO: 3) and SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4), in which the top graph is a chromatogram detected by a UV at 215 nm and the bottom graph is a base peak chromatogram.

*Page 5, please replace the paragraph starting on line 8, with the following amended paragraph:*

Fig. 10 A shows a peptide map of peptides obtained by the reduction/carboxymethylation of the humanized PM-1 antibody (Main) followed by trypsin digestion; Fig. 10 B shows the MS chromatogram of molecular weight of SLSLSPG (SEQ ID NO: 5) (selective monitoring at  $m/z$   $660.3 \pm 0.5$ ), Fig. 10 C shows that of SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4) (selective monitoring at  $m/z$   $602.3 \pm 0.5$ ), and Fig. 10 D shows that of SLSLSP (SEQ ID NO: 3) (selective monitoring at  $m/z$   $603.3 \pm 0.5$ ).

*Page 5, please replace the paragraph starting on line 26, with the following amended paragraph:*

Fig. 14 A shows a peptide map of peptides obtained by the reduction/carboxymethylation of the humanized PM-1 antibody subtype 1 followed by trypsin digestion; Fig. 14 B shows the MS chromatogram of molecular weight of SLSLSPG (SEQ ID NO: 5) (selective monitoring at  $m/z$   $660.3 \pm 0.5$ ), Fig. 14 C shows that of SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4) (selective monitoring at  $m/z$   $602.3 \pm 0.5$ ), and Fig. 14 D shows that of SLSLSP (SEQ ID NO: 3) (selective monitoring at  $m/z$   $603.3 \pm 0.5$ ).

*Page 6, please replace the paragraph starting on line 20, with the following amended paragraph:*

Fig. 21 A shows a peptide map of peptides obtained by the reduction/carboxymethylation of the humanized PM-1 antibody subtype 2 followed by trypsin digestion; Fig. 21 B shows the MS chromatogram of molecular weight of SLSLSPG (SEQ ID NO: 5) (selective monitoring at  $m/z$   $660.3 \pm 0.5$ ), Fig. 21 C shows that of SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4) (selective monitoring at  $m/z$   $602.3 \pm 0.5$ ), and Fig. 21 D shows that of SLSLSP (SEQ ID NO: 3) (selective monitoring at  $m/z$   $603.3 \pm 0.5$ ).

*Page 20, please replace the paragraph starting on line 26, with the following amended paragraph:*

As the materials, the native humanized PM-1 antibody (sometimes referred to as Main), the subtypes 1 and 2 of said antibody, and, as the reference peptides, a peptide Ser-Leu-Ser-Leu-Ser-Pro (SLSLSP) (SEQ ID NO: 3) that is present at the C-terminal of the humanized PM-1 antibody and in which Gly at the C-terminal has been removed and a peptide SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4) in which the C-terminal Pro has been amidated were used. The peptide SLSLSP (SEQ ID NO: 3) and the amidated peptide SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4) were chemically synthesized. The humanized PM-1 antibody Main and the subtypes 1 and 2 of said antibody were obtained by subjecting the humanized PM-1 antibody obtained in Example 1 to a column chromatography and collecting and purifying it by the following method.

*Page 22, please replace the paragraph starting on line 13, with the following amended paragraph:*

Forty  $\mu$ l of each sample treated as above was subjected to the liquid chromatography-mass spectrometry (LC-MS/MS). For the reference peptide solutions, i.e. the SLSLSP (SEQ ID NO: 3) solution (SLSLSP (SEQ ID NO: 3) is dissolved in water to make 4  $\mu$ M) and the SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4) solution (SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4) is dissolved in water to make 4  $\mu$ M), 50  $\mu$ l is subjected to the liquid chromatography-mass spectrometry.

*Page 22, please replace the paragraph starting on line 33, with the following amended paragraph:*

(1) Measurement of the reference peptide fragments

(a) Measurement of the peptide fragment SLSLSP (SEQ ID NO: 3)

Fig. 1 to Fig. 3 show the result of liquid chromatography (LC)-mass spectrometry (MS) of the peptide fragment SLSLSP (SEQ ID NO: 3). The top of Fig. 1 shows a chromatogram detected with a UV at 215 nm, and the bottom shows a chromatogram of a base peak chromatogram. Fig. 2 shows a mass spectrum, and Fig. 3 shows a zoom scan spectrum. The molecular weight (602.2) obtained was in close agreement with the theoretical value (602.3; monoisotopic molecular weight) (Fig. 2 and Fig. 3).

*Page 23, please replace the paragraph starting on line 8, with the following amended paragraph:*

(b) Measurement of the peptide fragment SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4)

Fig. 4 to Fig. 6 show the result of liquid chromatography (LC)-mass spectrometry (MS) of the peptide fragment SLSLSP (SEQ ID NO: 3). The top of Fig. 4 shows a chromatogram detected with a UV at 215 nm, and the bottom shows a chromatogram of a base peak chromatogram. Fig. 5 shows a mass spectrum, and Fig. 6 shows a zoom scan spectrum. The molecular weight (601.2) obtained was in close agreement with the theoretical value (601.3; monoisotopic molecular weight) (Fig. 5 and Fig. 6).

*Page 23, please replace the paragraph starting on line 18, with the following amended paragraph:*

(c) Measurement of the mixture of the peptide fragments SLSLSP (SEQ ID NO: 3) and SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4)

Fig. 7 to Fig. 9 show the result of liquid chromatography (LC)-mass spectrometry (MS) of the mixture of the peptide fragment SLSLSP (SEQ ID NO: 3) and SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4). The top of Fig. 7 shows a chromatogram detected with a UV at 215 nm, and the bottom shows a

chromatogram of a base peak chromatogram. Fig. 8 shows the mass spectrum of a peak at a retention time of 44 minutes in Fig. 7, and Fig. 9 shows the mass spectrum of a peak at a retention time of 51 minutes in Fig. 7. The both peptide fragments were completely separated under the condition of the above liquid chromatography.

*Page 23, please replace the paragraph starting on line 35, with the following amended paragraph:*

Fig. 10 A shows a peptide map of peptides obtained by the reduction/carboxymethylation of the humanized PM-1 antibody (Main) followed by trypsin digestion. In order to investigate the structure of the C-terminal fragment of the H chain, the MS chromatogram of SLSLSPG (SEQ ID NO: 5) (selective monitoring at  $m/z$  660.3 $\pm$ 0.5) is shown in Fig. 10 B, that of SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4) (selective monitoring at  $m/z$  602.3 $\pm$ 0.5) in Fig. 10 C, and that of SLSLSP (SEQ ID NO: 4) (selective monitoring at  $m/z$  603.3 $\pm$ 0.5) in Fig. 10 D. A peak corresponding to SLSLSPG (SEQ ID NO: 5) was detected at 49.7 minutes, but no peptide fragments having the molecular weight of SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4) and SLSLSP (SEQ ID NO: 3) were found.

*Page 24, please replace the paragraph starting on line 10, with the following amended paragraph:*

Fig. 11 to Fig. 13 show the result of LC-MS/MS analysis of a peptide obtained by the reduction/carboxymethylation of the humanized PM-1 antibody (Main) followed by trypsin digestion. The top in Fig. 11 shows a chromatogram detected by a UV at 215 nm and the bottom shows a base peak chromatogram. Fig. 12 shows a mass spectrum of the peak at a retention time of 50 minutes in Fig. 11, and Fig. 13 shows a zoom scan spectrum of the same peak as in Fig. 11. From these results, the detected peak was shown to have the amino acid sequence SLSLSPG (SEQ ID NO: 5). Thus, it was demonstrated that both C-terminals of the H chain of the humanized PM-1 antibody (Main) have the -SLSLSPG (SEQ ID NO: 5) sequence.

*Page 24, please replace the paragraph starting on line 25, with the following amended paragraph:*

Fig. 14 A shows a peptide map of peptides obtained by the reduction/carboxymethylation of the humanized PM-1 antibody subtype 1 followed by trypsin digestion. In order to investigate the structure of the C-terminal fragment of the H chain, Fig. 14 B shows the MS chromatogram of molecular weight of SLSLSPG (SEQ ID NO: 5) (selective monitoring at  $m/z$   $660.3 \pm 0.5$ ). Fig. 14 C shows that of SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4) (selective monitoring at  $m/z$   $602.3 \pm 0.5$ ), and Fig. 14 D shows that of SLSLSP (SEQ ID NO: 3) (selective monitoring at  $m/z$   $603.3 \pm 0.5$ ). In addition to a peak corresponding to SLSLSPG (SEQ ID NO: 5) at 47.7 minutes, a peak corresponding to SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4) at 46.2 minutes was noted (though a peak with a molecular weight of 603.3 was noted at about 46 minutes in Fig. 14 D, it is not SLSLSP (SEQ ID NO: 3), based on the retention time).

*Page 25, please replace the paragraph starting on line 22, with the following amended paragraph:*

From these results, the detected peak was shown to have the amino acid sequences SLSLSPG (SEQ ID NO: 5) and SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4). Thus, it was demonstrated that one of the H chain C-terminals of the humanized PM-1 antibody subtype 1 has the -SLSLSPG sequence (SEQ ID NO: 5), and the other has the -SLSLSPG-NH<sub>2</sub> sequence (SEQ ID NO: 6).

*Page 25, please replace the paragraph starting on line 30, with the following amended paragraph:*

Fig. 21 A shows a peptide map of peptides obtained by the reduction/carboxymethylation of the humanized PM-1 antibody subtype 2 followed by trypsin digestion. In order to investigate the structure of the C-terminal fragment of the H chain, Fig. 21 B shows the MS chromatogram of molecular weight of SLSLSPG (SEQ ID NO: 5) (selective monitoring at  $m/z$   $660.3 \pm 0.5$ ), Fig. 21 C shows that of SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4) (selective monitoring at  $m/z$   $602.3 \pm 0.5$ ), and Fig. 21 D shows that of SLSLSP (SEQ ID NO: 3) (selective monitoring at  $m/z$   $603.3 \pm 0.5$ ). Though a peak

corresponding to SLSLSPG (SEQ ID NO: 5) was slightly detected, a peak corresponding to SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4) was more strongly noted (though a peak with a molecular weight of 603.3 was noted at about 45 minutes in Fig. 21 D, it is not SLSLSP (SEQ ID NO: 3), based on the retention time).

*Page 26, please replace the paragraph starting on line 7, with the following amended paragraph:*

Fig. 22 to Fig. 24 show the result of LC-MS/MS analysis of a peptide obtained by the reduction/carboxymethylation of the humanized PM-1 antibody subtype 2 followed by trypsin digestion. In Fig. 22, the top is a chromatogram detected by a UV at 215 nm and the bottom is a base peak chromatogram. Fig. 23 shows a mass spectrum of the peak at a retention time of 45 minutes in Fig. 22, and Fig. 24 shows a zoom scan spectrum of the same peak as in Fig. 23. From these results, the detected peak was shown to have the amino acid sequence SLSLSP-NH<sub>2</sub> (SEQ ID NO: 4). Thus, it was demonstrated that both of the H chain C-terminals of the humanized PM-1 antibody subtype 2 have the -SLSLSPG-NH<sub>2</sub> sequence (SEQ ID NO: 6).